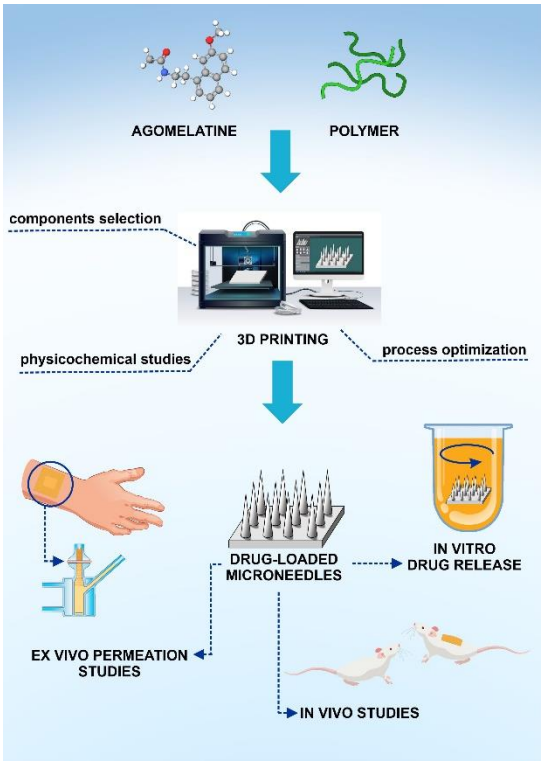
3D printing as a tool to obtain transdermal microneedle systems for improved efficiency in the treatment of depressive disorders

A few decades ago depression was reffered to as a short-term disease that required short-term treatment. Currently, it is being defined as a recurrent, long-term illness. **The data provided by the Polish National Health Fund at the beginning of 2020 show that almost 3% of Poles suffer from depression and other accompanying diseases.** According to the reports presented by World Health Organization (WHO) there are more than 264 million people affected with the disease worldwide. Unfortunately, due to low patients compliance the risk of recurrence is estimated to be about 80%. **Currently, almost all antidepressants are administered in the form of oral tablets. This route of administration is characterized by many disadvantages, such as insufficient effectiveness, numerous side-effects, multiple daily dosing and thus lower patient acceptance often leading to discontinuation of the therapy. Therefore, a lot of effort is focused on more advantageous delivery routes, among which the most popular is transdermal.** Since the first applications, transdermal drug delivery has contributed to remarkable progress in therapies of various diseases. However, in the case of antidepressants there is still much to discover until it can be considered as an alternative or substitution to the oral route.



One of the techniques that gives entirely new possibilities to develop very advanced and precise tools for drug delivery, including transdermal, is 3D printing. It offers a key for entirely new era of pharmaceutical dosage forms with complex structures and dimensions to meet the individual needs of patients, improving efficiency and safety of the therapy. Although the progress in introducing 3D printing to pharmaceutical sciences is enormous, it can be considered that it is only a fledgling field, with great potential, but also with a very large number of unknowns to be solved. The project will be a response for the growing need to design innovative transdermal drug delivery systems for antidepressants in order to provide more effective, safer and more precise therapy.

The main target of the project is to design and fabricate agomelatine-loaded microneedle systems with the use of 3D printing technique. The obtained systems will be examined in detail to verify how the composition and conditions during the manufacturing process affect their physicochemical properties, and further, how they translate into various pharmaceutical parameters *in vitro* and *in vivo*. One of the goals will be to verify whether the microneedle systems can be more efficient in reaching and keeping the blood drug levels, than traditional oral tablets, and if they can be regarded as an advantageous alternative.

The project will be divided into four main areas, intertwining and complementing each other, including ***i*. development of the manufacturing process and evaluation of mechanical properties, *ii*. analysis of physicochemical properties, *iii*. evaluation of pharmaceutical parameters, *iv*. assessment of bioavailability and therapeutic effectiveness in animal models.**

The results obtained in the project will provide very important information on how the conditions used in the process of creating microneedle systems, taking into account their different material composition and the presence of a the drug, affect the physicochemical parameters. On other hand, the obtained data are expected to show how the above-mentioned parameters may affect the crucial therapeutic properties and effectiveness of the therapy. **In the project, the main emphasis will be focused on detailed basic research in the field of material engineering, however the complex approach, especially in terms of *in vivo* research, will provide the basis for defining some principles that should be followed in the development of 3D printed micro-needle transdermal systems.** The experiments in animals will be performed to demonstrate that due to the use of microneedles it will be possible to use smaller doses, while maintaining the same or better effectiveness.